

Fungicidal composition comprising a pyridylmethylbenzamide derivative and a sulfamide derivative

5 The present invention relates to novel fungicidal compositions comprising a pyridylmethylbenzamide derivative and a sulfamide derivative. The present invention also relates to a method of combating phytopathogenic fungi by applying at a locus infested or liable to be infested such a composition.

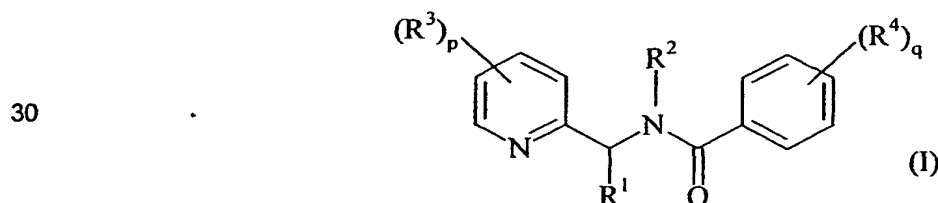
10 European patent application EP-A-1056723 generically discloses the possibility of combining pyridylmethylbenzamide derivatives with known fungicidal products to develop a fungicidal activity.

International patent application WO 02/069713 discloses fungicidal mixtures comprising a pyridylmethylbenzamide derivative and phosphorous acid or one of its
15 derivatives.

Some of the above mentioned mixtures have shown a synergistic effect. Nevertheless, it is always of high-interest in agriculture to use novel pesticidal mixtures showing a synergistic effect in order to avoid or to control the development of resistant strains to the active ingredients or to the mixtures of known active
20 ingredients used by the farmer while minimising the doses of chemical products spread in the environment and reducing the cost of the treatment.

We have now found some novel fungicidal compositions which possess the above mentioned characteristics.

25 Accordingly, the present invention relates to a composition comprising :
a) a pyridylmethylbenzamide derivative of general formula (I)



in which :

- R¹ may be a hydrogen atom, an optionally substituted alkyl group or an
35 optionally substituted acyl group;

- R² may be a hydrogen atom or an optionally substituted alkyl group;

- R³ and R⁴ may be chosen independently from each other as being a halogen atom, a hydroxyl group, a cyano group, a nitro group, -SF₅, a trialkylsilyl group, an optionally substituted amino group, an acyl group, or a group E, OE or SE, in which E may be an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl or a heterocyclyl group each of which may optionally be substituted;

- p represents 0, 1, 2, 3 or 4;

- q represents 0, 1, 2, 3 or 4;

and its agriculturally acceptable optical and/or geometric isomers, tautomers and addition salts with an acid or a base;

and

b) N-dichlorofluoromethylthio-N',N'-dimethyl-N-p-tolylsulfamide;

in a (a) / (b) weight ratio of from 0.01 to 10.

N-dichlorofluoromethylthio-N',N'-dimethyl-N-p-tolylsulfamide is a sulfamide derivative fungicide also known as tolylfluanid.

In the context of the present invention :

- the term halogen means bromine, chlorine, iodine or fluorine;

- the term alkyl means a linear or branched saturated hydrocarbon group containing from 1 to 6 carbon atoms;

- the term alkenyl means a linear or branched hydrocarbon group containing from 2 to 6 carbon atoms and an unsaturation in the form of double bond;

- the term alkynyl means a linear or branched hydrocarbon group containing from 2 to 6 carbon atoms and an unsaturation in the form of a triple bond;

- the term alkoxy means a linear or branched alkyloxy group containing from 1 to 6 carbon atoms;

- the term acyl means a formyl group or linear or branched alkoxycarbonyl group containing from 2 to 6 carbon atoms;

- the term cycloalkyl means a saturated cyclic hydrocarbon group containing from 3 to 8 carbon atoms;

- the term aryl means a phenyl or naphthyl group;

- the term heterocyclyl means saturated, partially saturated, unsaturated or aromatic cyclic group containing from 3 to 8 atoms, which may be a carbon atom, a nitrogen atom, a sulphur atom or an oxygen atom. Examples of such heterocyclyl may be pyridyl, pyridinyl, quinolyl, furyl, thienyl, pyrrolyl, oxazolynyl;

- the term "optionally substituted " means that the group thus termed may be substituted with one or more groups which may be halogen, alkyl, alkoxy, hydroxyl, nitro, amin, cyano or acyl.

5 The composition according to the present invention provides a synergistic effect. This synergistic effect allows a reduction of the chemical substances spread into the environment and a reduction of the cost of the fungal treatment.

 In the context of the present invention, the term "synergistic effect" is defined by Colby according to the article entitled "Calculation of the synergistic and
10 antagonistic responses of herbicide combinations" Weeds, (1967), 15, pages 20-22.

 The latter article mentions the formula:

$$E = x + y - \frac{x * y}{100}$$

 in which E represents the expected percentage of inhibition of the disease for the combination of the two fungicides at defined doses (for example equal to x and y
15 respectively), x is the percentage of inhibition observed for the disease by the compound (I) at a defined dose (equal to x), y is the percentage of inhibition observed for the disease by the compound (II) at a defined dose (equal to y). When the percentage of inhibition observed for the combination is greater than E, there is a synergistic effect.

20 In the context of the present invention, the term "synergistic effect" also means the effect defined by application of the Tammes method, "Isoboles, a graphic representation of synergism in pesticides", Netherlands Journal of Plant Pathology, 70(1964), pages 73-80.

25

 The composition according to the present invention comprises a pyridylmethylbenzamide derivative of general formula (I).

 Preferably, the present invention relates to a composition comprising a pyridylmethylbenzamide derivative of general formula (I) in which the different
30 characteristics may be chosen alone or in combination as being :

 - as regards R¹ and R², R¹ and R² may be chosen independently from each other as being a hydrogen atom or an optionally substituted alkyl group. More preferably, R¹ and R² may be chosen independently from each other as being a hydrogen atom, a methyl group or an ethyl group. Even more preferably, R¹ and R²
35 may be both hydrogen atoms.

- as regards R^3 and R^4 , R^3 and R^4 may be chosen independently from each other as being a halogen atom, a hydroxyl group, a nitro group, an optionally substituted amino group, an acyl group, or a group E, OE or SE, in which E may be a alkyl, a cycloalkyl, a phenyl or a heterocyclyl group, each of which may optionally be substituted. More preferably, R^3 and R^4 may be chosen independently from each other as being a halogen atom, a nitro group or a halogenoalkyl group. Even more preferably R^3 and R^4 may be chosen independently from each other as being a chlorine atom, a nitro group or a trifluoromethyl group.

- as regards p, p may be 1 or 2. More preferably, p may be 2.
- as regards q, q may be 1 or 2. More preferably, q may be 2;
and its agriculturally acceptable possible tautomers and addition salts with an acid or a base.

More preferably, the pyridylmethylbenzamide derivative of general formula (I) present in the composition of the present invention is :

- a compound (Ia) which is 2,6-dichloro-N-{{3-chloro-5-(trifluoromethyl)-2-pyridinyl}methyl}benzamide; or
- a compound (Ib) which is N-{{3-chloro-5-(trifluoromethyl)-2-pyridinyl}methyl}-2-fluoro-6-nitrobenzamide; or
- a compound (Ic) which is N-{{3-chloro-5-(trifluoromethyl)-2-pyridinyl}methyl}-2-methyl-6-nitrobenzamide;

and its agriculturally acceptable possible tautomers and addition salts with an acid or a base.

The composition according to the present invention comprises at least a pyridylmethylbenzamide derivative of general formula (I) (a) and tolylfluanid (b) in an (a) / (b) weight ratio of from 0.01 to 10; preferably of from 0.05 to 0.5; even more preferably, of from 0.1 to 0.2.

The composition of the present invention may further comprise a third fungicide active ingredient (c).

The third fungicidal active ingredient may preferably be selected from phosphorous acid derivative, phosphorous acid itself, or alkali metal, alkaline-earth metal or metallic salts thereof. More preferably, the additional fungicidal compound may be chosen as being ethyl hydrogen phosphonate.

Ethyl hydrogen phosphonate is a fungicidal compound also known as Fosetyl-Al.

Where the third active ingredient (c) as defined above is present in the composition, this compound may be present in an amount of (a) : (b) : (c) weight ratio of from 0.01 : 1 : 0.1 to 10 : 1 : 10; the ratios of compound (a) and compound (c) varying independently from each other. Preferably, the (a) : (b) : (c) weight ratio may be of from 0.05 : 1 : 0.5 to 0.5 : 1 : 5; more preferably of from 0.1 : 1 : 1 to 0.2 : 1 : 4.

The composition according to the present invention may further comprise an other additional component such as an agriculturally acceptable support, carrier or filler.

In the present specification, the term "support" denotes a natural or synthetic, organic or inorganic material with which the active material is combined to make it easier to apply, notably to the parts of the plant. This support is thus generally inert and should be agriculturally acceptable. The support may be a solid or a liquid. Examples of suitable supports include clays, natural or synthetic silicates, silica, resins, waxes, solid fertilisers, water, alcohols, in particular butanol, organic solvents, mineral and plant oils and derivatives thereof. Mixtures of such supports may also be used.

The composition may also comprise other additional components. In particular, the composition may further comprise a surfactant. The surfactant can be an emulsifier, a dispersing agent or a wetting agent of ionic or non-ionic type or a mixture of such surfactants. Mention may be made, for example, of polyacrylic acid salts, lignosulphonic acid salts, phenolsulphonic or naphthalenesulphonic acid salts, polycondensates of ethylene oxide with fatty alcohols or with fatty acids or with fatty amines, substituted phenols (in particular alkylphenols or arylphenols), salts of sulphosuccinic acid esters, taurine derivatives (in particular alkyl taurates), phosphoric esters of polyoxyethylated alcohols or phenols, fatty acid esters of polyols, and derivatives of the above compounds containing sulphate, sulphonate and phosphate functions. The presence of at least one surfactant is generally essential when the active material and/or the inert support are water-insoluble and when the vector agent for the application is water. Preferably, surfactant content may be comprised between 5% and 40% by weight of the composition.

Additional components may also be included, e.g. protective colloids, adhesives, thickeners, thixotropic agents, penetration agents, stabilisers, sequestering agents. More generally, the active materials can be combined with any solid or liquid additive, which complies with the usual formulation techniques.

5 In general, the composition according to the invention may contain from 0.05 to 99% (by weight) of active material, preferably 10 to 70% by weight.

Compositions according to the present invention can be used in various forms such as aerosol dispenser, capsule suspension, cold fogging concentrate, dustable powder, emulsifiable concentrate, emulsion oil in water, emulsion water in oil,
10 encapsulated granule, fine granule, flowable concentrate for seed treatment, gas (under pressure), gas generating product, granule, hot fogging concentrate, macrogranule, microgranule, oil dispersible powder, oil miscible flowable concentrate, oil miscible liquid, paste, plant rodlet, powder for dry seed treatment, seed coated with a pesticide, soluble concentrate, soluble powder, solution for seed
15 treatment, suspension concentrate (flowable concentrate), ultra low volume (ulv) liquid, ultra low volume (ulv) suspension, water dispersible granules or tablets, water dispersible powder for slurry treatment, water soluble granules or tablets, water soluble powder for seed treatment and wettable powder.

These compositions include not only compositions which are ready to be
20 applied to the plant or seed to be treated by means of a suitable device, such as a spraying or dusting device, but also concentrated commercial compositions which must be diluted before they are applied to the crop.

The fungicidal compositions of the present invention can be used to curatively
25 or preventively control the phytopathogenic fungi of crops. Thus, according to a further aspect of the present invention, there is provided a method for preventively or curatively controlling phytopathogenic fungi of crops characterised in that a fungicidal composition as hereinbefore defined is applied to the seed, the plant and/or to the fruit of the plant or to the soil in which the plant is growing or in which it is desired to grow.

30 The composition as used against phytopathogenic fungi of crops comprises an effective and non-phytotoxic amount of an active material of general formula (I).

The expression "effective and non-phytotoxic amount" means an amount of composition according to the invention which is sufficient to control or destroy the
35 fungi present or liable to appear on the crops, and which does not entail any appreciable symptom of phytotoxicity for the said crops. Such an amount can vary within a wide

range depending on the fungus to be combated, the type of crop, the climatic conditions and the compounds included in the fungicidal composition according to the invention.

This amount can be determined by systematic field trials, which are within the capabilities of a person skilled in the art.

5 The method of treatment according to the present invention is useful to treat propagation material such as tubers or rhizomes, but also seeds, seedlings or seedlings pricking out and plants or plants pricking out. This method of treatment can also be useful to treat roots. The method of treatment according to the present invention can also be useful to treat the overground parts of the plant such as trunks,
10 stems or stalks, leaves, flowers and fruits of the concerned plant.

Among the plants that can be protected by the method according to the invention, mention may be made of cotton; flax; vine; fruit or vegetables crops such as *Rosaceae sp.* (for instance pip fruits such as apples and pears, but also stone fruits such as apricots, almonds and peaches), *Ribesioideae sp.*, *Juglandaceae sp.*,
15 *Betulaceae sp.*, *Anacardiaceae sp.*, *Fagaceae sp.*, *Moraceae sp.*, *Oleaceae sp.*, *Actinidaceae sp.*, *Lauraceae sp.*, *Musaceae sp.* (for instance banana trees and plantains), *Rubiaceae sp.*, *Theaceae sp.*, *Sterculiaceae sp.*, *Rutaceae sp.* (for instance lemons, oranges and grapefruits); leguminous crops such as *Solanaceae sp.* (for instance tomatoes), *Liliaceae sp.*, *Asteraceae sp.* (for instance lettuces), *Umbelliferae sp.*, *Cruciferae sp.*, *Chenopodiaceae sp.*, *Cucurbitaceae sp.*, *Papilionaceae sp.* (for instance peas), *Rosaceae sp.* (for instance strawberries); big crops such as *Graminae sp.* (for instance maize, lawn or cereals such as wheat, rice, barley and triticales), *Asteraceae sp.* (for instance sunflower), *Cruciferae sp.* (for instance colza), *Papilionaceae sp.* (for instance soja), *Solanaceae sp.* (for instance potatoes),
20 *Chenopodiaceae sp.* (for instance beetroots); horticultural and forest crops; as well as
25 genetically modified homologues of these crops.

Among the plants and the possible diseases of these plants protected by the method according to the present invention, mention may be made of :

- wheat, as regards controlling the following seed diseases: fusaria
30 (*Microdochium nivale* and *Fusarium roseum*), stinking smut (*Tilletia caries*, *Tilletia controversa* or *Tilletia indica*), septoria disease (*Septoria nodorum*) and loose smut;
- wheat, as regards controlling the following diseases of the aerial parts of the plant: cereal eyespot (*Tapesia yallundae*, *Tapesia acuiformis*), take-all (*Gaeumannomyces graminis*), foot blight (*F. culmorum*, *F. graminearum*), black speck
35 (*Rhizoctonia cerealis*), powdery mildew (*Erysiphe graminis forma specie tritici*), rusts

(*Puccinia striiformis* and *Puccinia recondita*) and septoria diseases (*Septoria tritici* and *Septoria nodorum*);

- wheat and barley, as regards controlling bacterial and viral diseases, for example barley yellow mosaic;

5 - barley, as regards controlling the following seed diseases: net blotch (*Pyrenophora graminea*, *Pyrenophora teres* and *Cochliobolus sativus*), loose smut (*Ustilago nuda*) and fusaria (*Microdochium nivale* and *Fusarium roseum*);

 - barley, as regards controlling the following diseases of the aerial parts of the plant: cereal eyespot (*Tapesia yallundae*), net blotch (*Pyrenophora teres* and *Cochliobolus sativus*), powdery mildew (*Erysiphe graminis forma specie hordei*),
10 dwarf leaf rust (*Puccinia hordei*) and leaf blotch (*Rhynchosporium secalis*);

 - potato, as regards controlling tuber diseases (in particular *Helminthosporium solani*, *Phoma tuberosa*, *Rhizoctonia solani*, *Fusarium solani*), mildew (*Phytophthora infestans*) and certain viruses (virus Y);

15 - potato, as regards controlling the following foliage diseases: early blight (*Alternaria solani*), mildew (*Phytophthora infestans*);

 - cotton, as regards controlling the following diseases of young plants grown from seeds: damping-off and collar rot (*Rhizoctonia solani*, *Fusarium oxysporum*) and black root rot (*Thielaviopsis basicola*);

20 - protein yielding crops, for example peas, as regards controlling the following seed diseases: anthracnose (*Ascochyta pisi*, *Mycosphaerella pinodes*), fusaria (*Fusarium oxysporum*), grey mould (*Botrytis cinerea*) and mildew (*Peronospora pisi*);

 - oil-bearing crops, for example rape, as regards controlling the following
25 seed diseases: *Phoma lingam*, *Alternaria brassicae* and *Sclerotinia sclerotiorum*;

 - corn, as regards controlling seed diseases: (*Rhizopus* sp., *Penicillium* sp., *Trichoderma* sp., *Aspergillus* sp., and *Gibberella fujikuroi*);

 - flax, as regards controlling the seed disease: *Alternaria linicola*;

 - forest trees, as regards controlling damping-off (*Fusarium oxysporum*,
30 *Rhizoctonia solani*);

 - rice, as regards controlling the following diseases of the aerial parts: blast disease (*Magnaporthe grisea*), bordered sheath spot (*Rhizoctonia solani*);

 - leguminous crops, as regards controlling the following diseases of seeds or of young plants grown from seeds: damping-off and collar rot (*Fusarium oxysporum*,
35 *Fusarium roseum*, *Rhizoctonia solani*, *Pythium* sp.);

- leguminous crops, as regards controlling the following diseases of the aerial parts: grey mould (*Botrytis* sp.), powdery mildews (in particular *Erysiphe cichoracearum*, *Sphaerotheca fuliginea* and *Leveillula taurica*), fusaria (*Fusarium oxysporum*, *Fusarium roseum*), leaf spot (*Cladosporium* sp.), alternaria leaf spot
5 (*Alternaria* sp.), anthracnose (*Colletotrichum* sp.), septoria leaf spot (*Septoria* sp.), black speck (*Rhizoctonia solani*), mildews (for example *Bremia lactucae*, *Peronospora* sp., *Pseudoperonospora* sp., *Phytophthora* sp.);

- fruit trees, as regards diseases of the aerial parts: monilia disease (*Monilia fructigenae*, *M. laxa*), scab (*Venturia inaequalis*), powdery mildew (*Podosphaera*
10 *leucotricha*);

- vine, as regards diseases of the foliage: in particular grey mould (*Botrytis cinerea*), powdery mildew (*Uncinula necator*), black rot (*Guignardia biwelli*) and mildew (*Plasmopara viticola*);

- beetroot, as regards the following diseases of the aerial parts: cercospora blight
15 (*Cercospora beticola*), powdery mildew (*Erysiphe beticola*), leaf spot (*Ramularia beticola*).

Preferably, the plant that can be protected by the method according to the present invention is vine.

20 The fungicidal composition according to the present invention may also be used against fungal diseases liable to grow on or inside timber. The term "timber" means all types of species of wood, and all types of working of this wood intended for construction, for example solid wood, high-density wood, laminated wood, and plywood. The method for treating timber according to the invention mainly consists
25 in contacting one or more compounds of the present invention, or a composition according to the invention; this includes for example direct application, spraying, dipping, injection or any other suitable means.

The dose of active material usually applied in the treatment according to the
30 present invention is generally and advantageously between 10 and 2000 g/ha, preferably between 50 and 1500 g/ha for applications in foliar treatment. The dose of active substance applied is generally and advantageously between 2 and 200 g per 100 kg of seed, preferably between 3 and 150 g per 100 kg of seed in the case of seed treatment. It is clearly understood that the doses indicated above are given as
35 illustrative examples of the invention. A person skilled in the art will know how to adapt the application doses according to the nature of the crop to be treated.

The fungicidal composition according to the present invention may also be used in the treatment of genetically modified organisms with the compounds according to the invention or the agrochemical compositions according to the invention. Genetically modified plants are plants into whose genome a heterologous gene encoding a protein of interest has been stably integrated. The expression "heterologous gene encoding a protein of interest" essentially means genes which give the transformed plant new agronomic properties, or genes for improving the agronomic quality of the transformed plant.

10

The compositions according to the present invention may also be used for the preparation of composition useful to curatively or preventively treat human and animal fungal diseases such as, for example, mycoses, dermatoses, trichophyton diseases and candidiasis or diseases caused by *Aspergillus spp.*, for example *Aspergillus fumigatus*.

15

The present invention will now be illustrated by way of the following examples.

20 **Example : treatment of vine with a composition according to the invention**

This example demonstrates a synergy for a mixture of 2,6-dichloro-N-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide (compound Ia) and tolylfluanid on Vine downy mildew (*Plasmopara Viticola*) in 72h preventive application on tomato.

25

Vine plants (Cabernet -Sauvignon variety) were grown in a sandy soil in plastic pots with a single plant per pot. At the age of 2 months (6 to 7 leaves developed), these plants were sprayed with the two fungicides either alone or in a mixture. Fungicide compounds applied in mixtures were also applied singly at the same doses as those used in the combinations. The fungicide compounds, either alone or in mixtures, were applied at a volume rate of 250 l water per ha .

30

Three weight ratios of the mixture of compound Ia / tolylfluanid have been studied : 1/5, 1/6.67 and 1/10.

35

Starting with compound Ia in the form of suspension concentrate (SC) at 480g/l and tolylfluanid in the form of Water Dispersible Granules (WG) 500g/kg (Euparene), plant protection mixtures for application corresponding to a volume of 250 l of liquid per ha are prepared.

5 The dose range of compound Ia corresponds to 1.56 mg/l, 12.5 mg/l, 25 mg/l, 50 mg/l and 75 mg/l.

Three days after treatment, each plant was inoculated by spraying an aqueous suspension of sporangia of *Plasmopara viticola* obtained from contaminated leaves.
10 The concentration of sporangia was about 100,000 units per ml.

After contamination the plants were incubated for two days at 18°C in a saturated atmosphere and then for 5 days at about 20°C with 90-100% relative humidity.

15 Seven days after contamination, symptoms were evaluated in terms of the extent of the lower surface of the leaves infected, in comparison with untreated but contaminated plants.

The efficacy of the treatment was calculated using the Abbott formula :

20
$$\text{Efficacy} = (\text{Untreated} - \text{Treated} / \text{Untreated}) \times 100$$

The concentrations of the fungicide compounds alone or in a mixture giving 50%, 70% and 90% efficacy for each component were determined based on the sigmoid curve dose / response model with their confidence intervals.

25 The analyses of the results were carried out using the TAMMES model (Isoboles, a graphic representation of synergism in pesticides, Neth.J. Plant Path. 70 (1964): 73-80) or Colby model.

The results obtained are presented in the form of point values, corresponding to 50%, 70% or 90% control of the pathogen and placed in a Tammes isobole diagram which comprises on the x-axis the doses of Compound Ia expressed in mg/l
30 and on the y-axis the doses of tolylfluanid also in mg/l.

The calculated results corresponding to ED50, ED70 and ED90 (effective doses providing 50%, 70% and 90% of disease control) for the various ratios of the mixtures that have been evaluated are presented in the following Table 1, 2 and 3.

Compound Ia : tolyfluanid ratio	1 : 5	1 : 6.67	Compound Ia alone	Tolyfluanid alone
Practical doses for 50% efficacy (in mg/l)	7.6 38	7.3 48.7	15.7	140.7
Theoretical dose for 50% efficacy (in mg/l)	10.1 50.5	9 60	-	-

Table 1 : ED50

Compound Ia : tolyfluanid ratio	1 : 5	1 : 6.67	1 : 10	Compound Ia alone	Tolyfluanid alone
Practical doses for 70% efficacy (in mg/l)	13.5 67.5	12.4 82.7	11.5 115	27	231.4
Theoretical dose for 70% efficacy (in mg/l)	17.1 85.5	15.2 101.4	12.5 125	-	-

Table 2 : ED70

Compound Ia : tolyfluanid ratio	1 : 5	1 : 6.67	1 : 10	Compound Ia alone	Tolyfluanid alone
Practical doses for 90% efficacy (in mg/l)	34 38	28.3 48.7	23.3 74	65	533.6
Theoretical dose for 90% efficacy (in mg/l)	28.5 285	35.4 236.1	39.7 198.5	-	-

Table 3 : ED90

These results have been calculated on the basis of 3 repeats per factor according to the Tamme's method taking into account the product efficacy for a range of ratios and for method for 50%, 70% and 90% of disease control on tomato.

This preventive test on tomato late blight shows the synergism of the fungicide compositions containing compounds A and B at ratios equal to 1/5, 1/6.67 and 1/10. It has been demonstrated that less amount of both compounds are necessary to control 50%, 70% and 90% of the disease compared to the theoretical doses of each compounds expected in the mixture with just additional effect.

- A synergy of the above mixture is also demonstrated when data are analysed according to Colby method. Following Table 4 presents the results obtained based on using the Colby method for evaluating the synergy of the mixture of compound Ia with tolylfluanid according to the invention. Practical efficacy is superior to theoretical efficacy showing the synergism of the fungicide compositions containing compounds Ia and tolylfluanid at ratios equal to 1/5 , 1/6.67 and 1/10.

Dose of compound Ia (mg/l)	75	75	75	50	50	25	25	25	12.5	12.5	12.5	1.56
Dose of tolylfluanid (mg/l)	750	500	375	333.3	250	250	166.6	125	125	83.3	62.5	7.8
Practical efficacy (%)	99	99	99	97	94.4	93.2	92.7	83.8	77.2	60.8	65.8	11.4
Theoretical efficacy (%)	95	96	94	93	81	81	30	30	30.4	34.2	5.1	3.8

Table 3 : Synergism according to Colby method between compound Ia and tolylfluanid on vine downy mildew